PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Anthony Robert Milnes COATES

Appln. No.: 10/534,054

Confirmation No.: 2651

Filed: March 22, 2006

For: PAIN RELIEF AGENTS

Docket No: Q87779

Group Art Unit: 1645

Examiner: Rodney P SWARTZ

REQUEST FOR REFUND

MAIL STOP 16
Director of the U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant hereby respectfully requests a refund in the amount of $600.00. This refund is to be credited to Deposit Account No. 19-4880.

The total number of claims previously paid for was 25. The Amendment filed on August 1, 2008 contains a total of 28 claims. Our deposit account was erroneously charged for 15 claims in excess of 20 ($50 x 15 = $750). However the Amendment filed only increased the total claim count by 3 ($50 x 3 = $150). A copy of the Deposit Account Monthly Statement showing the charge to our account, and Amendment as filed are enclosed.

Respectfully submitted,

/Susan J. Mack/
Susan J. Mack
Registration No. 30,951

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: March 26, 2009

UNITED STATES PATENT AND TRADEMARK OFFICE

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9-30-08
Page
18

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DATE POSTED MO.	DAY	YR.	CONTROL NO.	DESCRIPTION (Serial, Patent, TM, Order)	DOCKET NO.	FEE CODE	CHARGES/ CREDITS	BALANCE
9	4	08	12928	12281669	Q109979	8021	40.00	202058.41
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AN AMOUNT SUFFICIENT TO COVER ALL SERVICES REQUESTED MUST ALWAYS BE ON DEPOSIT	OPENING BALANCE	TOTAL CHARGES	TOTAL CREDITS	CLOSING BALANCE

MS020F (7/2007)

*** O.D. INDICATES OVERDRAWN

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Filed: March 22, 2006

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Docket No: Q87779

Group Art Unit: 1645

Examiner: Rodney P SWARTZ

AMENDMENT UNDER 37 C.F.R. § 1.111

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Office Action dated April 7, 2008, please amend the above-identified application as follows on the accompanying pages.

TABLE OF CONTENTS

AMENDMENTS TO THE SPECIFICATION

Please replace the specification filed May 6, 2005, with the Substitute Specification submitted herewith.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1-28. (canceled).

29-30. (canceled).

31. (currently amended): The method of Claims ~~29~~34 or 35, wherein the heat shock polypeptide is derived from a bacterium.

32. (previously presented): The method of Claim 31, wherein the bacterium is a Mycobacterium.

33. (previously presented): The method of Claim 32, wherein the Mycobacterium is *Mycobacterium tuberculosis*.

34. (currently amended): A method of relieving pain comprising administering, to a subject in need thereof, a heat shock polypeptide or a nucleotide molecule encoding a heat shock polypeptide~~The method of any one of Claims 29 to 33~~,

wherein the heat shock polypeptide is a chaperonin,

wherein the nucleotide molecule comprises:

(i) at least one nucleotide sequence selected from the nucleotide sequence of SEQ ID NOs: 1, 3, and 5~~of Figure 1 and /or Figure 2 and/or Figure 3~~, or

(ii) a sequence which has ~~more than~~at least 66% identity to sequence (i)~~, or a sequence which hybridises to sequence (i) under conditions of 2 x SSC, 65°C (wherein SCC= 0.15M NaCl, 0.15M sodium citrate, pH 7.2), which~~

~~encodes a functionally equivalent polypeptide to the sequence encoded by the nucleotide sequence of Figure 1 and/or Figure 2 and/or Figure 3,~~ or

(iii) a fragment of ~~seqence~~ sequence (i) or (ii) encoding a functionally equivalent polypeptide fragment wherein the functionally equivalent polypeptide fragment is from 3 to 400 residues in length.

35. (currently amended): A method of relieving pain comprising administering, to a subject in need thereof, a heat shock polypeptide or a nucleotide molecule encoding a heat shock polypeptide~~The method of any one of Claim 29 or 30~~,

wherein the heat shock polypeptide is a chaperonin,

wherein the polypeptide comprises:

(i) at least one amino acid sequence selected from the amino acid sequence of SEQ ID NOs:2, 4, and 6~~Figure 1 and/or Figure 2 and/or Figure 3~~, or

(ii) a sequence which has ~~more than~~at least 60% identity to sequence (i) ~~which provides a functionally equivalent polypeptide,~~ or

(iii) a functionally equivalent fragment of sequence (i) or (ii) wherein the functionally equivalent fragment is from 3 to 400 residues in length.

36. (canceled).

37. (previously presented): The method of Claim 36, wherein the functionally equivalent fragment is from 3 to 100 residues in length.

38. (previously presented): The method of Claim 34, wherein the nucleotide molecule encodes a functionally equivalent polypeptide fragment.

39. (currently amended): The method of ~~Claim 29~~Claim 34 or 35, wherein ~~the a~~said heat shock polypeptide or ~~a~~said nucleotide molecule is administered in a composition comprising a pharmaceutically acceptable excipent, diluent or carrier.

40. (currently amended): The method of ~~Claim 29~~Claim 34 or 35, wherein ~~the a~~said heat shock polypeptide or ~~a~~ said nucleotide molecule is administered in a composition comprising at least one additive for assisting or augmenting the pain relief action ~~of~~ by the nucleotide molecule or polypeptide.

41. (previously presented): The method of Claim 40, wherein the additive is selected from at least one member of the group consisting of paracetamol, aspirin, ibuprofen, another non-steroidal anti-inflammatory drug (NSAID), a cylooxygenase-2-selective inhibitor (CSI), and an opiate.

42. (currently amended): The method of Claim 40, wherein the composition ~~is in a form which~~ provides prolonged or sustained pain relief.

43. (currently amended): The method of ~~Claim 29~~Claim 34 or 35, wherein said heat shock polypeptide or nucleotide molecule encoding a heat shock polypeptide are administered in single or divided doses at a daily dosage level of from 0.0001 to 100,000 mg.

44. (previously presented): The method of Claim 43, wherein said daily dosage level is from 0.0001 to 1000 mg.

45. (previously presented): The method of Claim 43, wherein the divided doses are administered between six and twelve hours apart.

46. (previously presented): The method of Claim 45, wherein the divided doses are administered between nine and twelve hours apart.

47. (previously presented): The method of Claim 43, wherein the divided doses are administered between twelve hours and twelve days apart.

48. (previously presented): The method of Claim 43, wherein the divided doses are administered between twelve days and six months apart.

49. (previously presented): The method of Claim 39, wherein the composition is formulated to permit administration by at least one route selected from the group consisting of intranasal, oral, parenteral, topical, ophthalmic, suppository, pessary and inhalation.

50. (previously presented): The method of Claim 49, wherein the composition is formulated to permit administration by inhalation.

51. (currently amended): The method of ~~Claim 29~~Claim 34 or 35, wherein the subject is a human or animal.

52. (previously presented): The method of Claim 51, wherein the subject is a human.

53. (currently amended): The method of ~~Claim 29~~Claim 34 or 35, wherein the pain is due to at least one member selected from the group consisting of backache, headache, toothache, earache, arthritis, gout, soft tissue trauma, ligament/tendon traumatic damage, a broken bone, cancer, post operative pain, menstrual pain, obstetric pain, renal tract pain, visceral pain, a burn, an abscess and an infection.

AMENDMENTS TO THE DRAWINGS

The attached sheets of drawings includes changes to Figures 4-9 in response to the Examiner's objections to the drawings. These Replacement Sheets, pages 6-11, replace the original sheets 6-11.

Attachment: 6 Replacement Sheets

REMARKS

Status of Claims and Amendment

Claims 31, 34, 35, 39, 40, 42, 43, 51 and 53 are amended. Claims 29 and 30 are canceled. Claims 29-53 are all the pending claims in this application. Claims 29-53 are rejected.

Claim 31 has been amended to change the claim dependency to claims 34 or 35.

Claim 34 has been amended to replace "hybridises" with "hybridizes" in response to an objection to the claims,

Claim 34 has been amended to replace "of Figure 1 and/or Figure 2 and/or Figure 3" with "of SEQ ID NOs: 1, 3, and 5", and claim 35 has been amended to replace "of Figure 1 and/or Figure 2 and/or Figure 3" with "of SEQ ID NOs: 2, 4, and 6". Support for the amendment to claims 34 and 35 may be found at least at page 4, line 29 to page 5, line 16 of the specification.

In addition, claims 34 and 35 have been amended to incorporate the limitations of claims 29, 30, and 36, and to delete reference to the conditions for hybridization.

Claims 39 and 40 have been amended to replace "the a" with "said" as suggested by the Office Action in response to a § 112, second paragraph rejection. In addition, claim 40 has been amended to recite "for assisting or augmenting the pain relief action by the nucleotide or polypeptide." Support for the amendment to claim 40 may be found at least at pages 3-4 of the specification.

Claim 42 has been amended to delete recitation to a "form."

Claims 43, 51 and 53 have been amended to change their dependency.

The specification has been replaced with a Substitute Specification in response to the objections to the specification by the Examiner. Specifically, the specification has been amended to correct for typographical errors in response to objections to the specification.

Figures 4-9 have been replaced with Replacement Sheets in response to the Examiner's objections to the drawings. Specifically, Figures 4 and 5 have been corrected to replace "CP.01" with "cpn 60.1", and Figures 6 and 7 have been corrected to replace "CP.02" with "cpn 60.2". In addition, Figures 8 and 9 have been corrected to replace "CPn 10" with "cpn 10". Support for the amendments to the drawings may be found at pages 9-10 of the specification.

No new matter is added.

Information Disclosure Statements

Applicants thank the Examiner for acknowledging the Information Disclosure Statements filed May 6, 2005 and March 22, 2006, by returning signed and initialed copies of the PTO SB/08 A & B forms submitted therewith.

Priority

Applicants thank the Examiner for acknowledging Applicants' claim of priority to GB Application No. 0226105.5 filed November 8, 2002, as well as receipt of a certified copy of the priority document.

Response To Objections to the Specification

At pages 2-3 of the Office Action, the Examiner objects to specifications for various informalities such as lack of priority statement in the first line of the specification, embedded hyperlinks and browser-executable codes, and spelling errors.

In response, Applicants submit herewith a Substitute Specification correcting these informalities.

Withdrawal of the grounds of objection is respectfully requested.

Response To Objections to the Drawings

At pages 3-4 of the Office Action, the Examiner objects to Figures 4 to 9 for errors in the figure legends.

In response, Applicants submit herewith Replacement Sheets for Figures 4 to 9 correcting these errors.

Withdrawal of the grounds of objection is respectfully requested.

Response To Claim Objections

Claim 34 is objected for spelling of "hybridises" and asked to change it to "hybridizes".

In response, Applicants have amended claim 34 to correct this typographical error.

Withdrawal of the grounds of objection is respectfully requested.

Response To Rejections Under 35 U.S.C. § 112, second paragraph

Claims 31-34 and 38 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for the reasons discussed below.

1. Claim 31 appears to be rejected for reciting that the heat shock polypeptide is "derived" from a bacterium.

In response, Applicants note that one of ordinary skill in the art would understand, based upon the specification and common vernacular used in the art, that "derived" is regularly used to indicate the origin of a particular biological material. For instance, a polynucleotide that has been cloned from the genome of a particular organism is often referred to as "derived" from that organism. Similarly, a polypeptide would be "derived" from a particular bacterium if it were directly isolated from the bacterium or if it was expressed from DNA cloned from the bacterium.

Withdrawal of the rejections under § 112, second paragraph, is respectfully requested.

2. Claims 34-38 appear to be rejected for referring to sequences "of Figure 1 and/or Figure 2 and/or Figure 3". The Office Action recommends SEQ ID NOs be inserted into the claims.

In response, claims 34 and 35 have been amended to replace "of Figure 1 and/or Figure 2 and/or Figure 3" with "of SEQ ID NOs: 1, 2, and 3". Accordingly, the rejection is rendered moot with regard to claims 36-38 which are directly or indirectly dependent on claims 34 or 35.

Withdrawal of the rejections under § 112, second paragraph, is respectfully requested.

3. Claims 39-50 appear to be rejected because claims 39 and 40 are dependent on claim 29, which recites that "the a heat shock polypeptide or a nucleotide molecule" is administered. The Office Action recommends that the wording be replaced with "wherein said heat shock polypeptide or said nucleotide molecule".

In response, claims 39 and 40 have been amended to replace "the a" with "said" as suggested. Accordingly, the rejection is rendered moot with regard to claims 41-50 which are directly or indirectly dependent on claims 29 or 40.

Withdrawal of the rejections under § 112, second paragraph, is respectfully requested.

4. Claims 40-48 appear to be rejected because claim 40 is drawn to a composition comprising at least one additive "for assisting or augmenting the action" of the nucleotide molecule or polypeptide. The Office Action asserts that the metes and bounds of "for assisting or augmenting the action" is unclear. For example, the Office Action asserts that it is unclear whether the additive augments the pain relief or absorption of the nucleotide or polypeptide into a subject.

In response, Applicants note that one of ordinary skill in the art would understand from reading the specification, e.g., at pages 3-4, that the additive augments the pain relief of the

nucleotide or polypeptide. Accordingly, solely to advance prosecution of the present application, claim 40 has been amended to recite "for assisting or augmenting the pain relief action by the nucleotide or polypeptide."

Withdrawal of the rejections under § 112, second paragraph, is respectfully requested.

5. Claim 42 appears to be rejected for the recitation that the composition is "in a form which provides prolonged or sustained pain relief". It is unclear what structural characteristics are encompassed by such a "form".

In response, Applicants note that claim 42 has been amended to delete recitation of a "form."

Withdrawal of the rejections under § 112, second paragraph, is respectfully requested.

Response To Rejections Under 35 U.S.C. 112, first paragraph

1. Claims 34-38 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for whole heat shock proteins, does not reasonably provide enablement for any/all fragments of said heat shock proteins providing pain relief.

The Office Action appears to assert that because the use of chaperonins for pain relief was not known, there is a lack of predictability in the art that chaperonins could be utilized for pain relief, and any fragments of said chaperonins were also not known to alleviate pain. In addition, the Office Action asserts that the specification does not provide sufficient guidance to encompass the scope of the instant claims, i.e., any fragment of any size utilized as pain relief. The Office Action appears to assert that the only examples in the specification utilize whole cpn 60.1, cpn 60.2 or cpn 10, and the specification does not teach which part of the whole sequence can be replaced and still retain all of its pain relief characteristic.

Thus, the Office Action appears to conclude that the amount of experimentation is undue, and merely constitutes an invitation to experiment with fragments of chaperonins, without a reasonable expectation of success.

In response, Applicants note that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. Further, even in the unpredictable arts, a disclosure of every operable species is not required. M.P.E.P. § 2164.03. We note that "because only an enabling disclosure is required, [Applicants] need not describe all actual embodiments." M.P.E.P. § 2164.02.

Further the Board of Patent Appeals and Interferences (BPAI) has stated that "[t]he amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art." *Ex parte Kubin* (B.P.A.I. 2007). In this regard, BPAI has recognized that mere routine experimentation is required to enable the full scope of an Applicants' claims reciting nucleic acids encoding proteins at least 80% identical to the disclosed amino acid sequence claimed. *Ex parte K4ubin* (B.P.A.I. 2007). Thus, the BPAI has found claims having scope broader than the exact amino acid or nucleotide sequence disclosed should not be rejected under the enablement requirement of 35 U.S.C. § 112, first paragraph. Also, "[t]he fact experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." M.P.E.P. §2164.01.

Applicants note that the structural characteristic of chaperonin 60 and chaperonin 10 are well-established in the art. (See page 2, lines 5-11 of the specification). In addition, *Mycobacterium tuberculosis* is known to produce chaperonin 60.1 (cpn 60.1), chaperonin 60.2

(cpn 60.2), and chaperonin 10 (cpn 10). (See page 2, lines 26-29 of the specification). In fact, the naming of chaperonin 60.1 is based upon its amino acid sequence identity with other known chaperonins. Id. Accordingly, chaperonin 60.2, or SEQ ID NO:4 and 3, respectively, is disclosed to exhibit 59.6% identity to the amino acid sequence of cpn 60.1 (SEQ ID NO:2), and 65.6% identity to the nucleic acid sequence of cpn 60.1 (SEQ ID NO:1). (See page 3, lines 1-2 and page 9, lines 10-14 of the specification). An assay to determine the pain relief activity of the claimed nucleotides and claimed is polypeptides is provided in Examples 2 and 3 and the results are illustrated in Figures 6 and 7 to show the reduction in hyperalgesia to endotoxin (or sensitivity to pain) as expressed by the duration of paw withdrawals.

Furthermore, as disclosed at page 8 of the present specification, one skilled in the art would understand and surmise based on common technical knowledge and the disclosure in the specification, e.g., determination of the percent identity in the amino acid sequence based on the GAP program, Clustal W program, FAST pairwise alignment program, BLOSUM, or even a BLAST search algorithm, in order to make and use the claimed nucleotides having at least 66% identity to sequence (i), and the claimed polypeptides having at least 60% or more identity to sequence (i).

Accordingly, Applicants note that because the action of proteins is often attributed to particular domains and the full length protein is not generally required for activity, it would be a matter of routine experimentation to test the claimed nucleotides and claimed polypeptides for their pain relief characteristics.

Reconsideration and withdrawal of the rejection under § 112, first paragraph, is respectfully requested.

2. Claims 29-53 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for relieving pain utilizing whole heat shock proteins, does not reasonably provide enablement for relieving pain by administration of polynucleotides encoding a heat shock polypeptide.

The reasons asserted by the Office Action appear to be similar to those discussed above. In other words, because using chaperonins or their nucleotides for pain relief is not known, there is a lack of predictability in the art that chaperonins may be used for pain relief. Also, the specification is asserted to provide insufficient guidance to enable the scope of the instant claims, i.e., administration of nucleotides encoding heat shock polypeptides for pain relief. The Office Action appears to assert that the only examples in the specification use whole cpn 60.1, cpn 60.2 or cpn 10 polypeptides, and do not teach which part of the whole sequence can be replaced and still retain all of its pain relief characteristic.

Thus, the Office Action appears to conclude that the amount of experimentation is undue, and merely constitutes an invitation to experiment with fragments of chaperonins, without a reasonable expectation of success.

For similar reasons discussed above, Applicants note that the specification provides ample guidance in combination with the common technical knowledge in the art to enable one of ordinary skill in the art to make and use the presently claimed invention.

Reconsideration and withdrawal of the rejection under § 112, first paragraph, is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Tu A. Phan/

Tu A. Phan, Ph.D.
Registration No. 30,951

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
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WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: August 1, 2008

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Anthony Robert Milnes COATES

Appln. No.: 10/534,054

Confirmation No.: 2651

Filed: March 22, 2006

For: PAIN RELIEF AGENTS

Docket No: Q87779

Group Art Unit: 1645

Examiner: Rodney P SWARTZ

PETITION FOR EXTENSION OF TIME UNDER 37 C.F.R. § 1.136

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. § 1.136, Applicant hereby petitions for an extension of time of one month, extending the time for responding to the Office Action of April 7, 2008 to August 7, 2008.

The statutory fee of $120.00 is being charged to Deposit Account No. 19-4880 via EFS Payment Screen. The USPTO is also directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Tu A. Phan/

Tu A. Phan, Ph.D.
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Group Art Unit: 1645

Examiner: Rodney P SWARTZ

DECLARATION REGARDING SUBSTITUTE SPECIFICATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith is a Substitute Specification (clean copy) and Substitute Specification (marked-up copy).

These versions were taken from an electronic version sent to the undersigned on behalf of the Inventors. While the pagination somewhat differs from the original Specification, the content is the same.

I further state that I have reviewed the changes in the Substitute Specification and do not believe any change constitutes new matter.

Respectfully submitted,

/Tu A. Phan/

Tu A. Phan, Ph.D.
Registration No. 59,392

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Date: August 1, 2008